

WHAT IS CLAIMED IS:

1. Use of a therapeutically effective amount of an IL-6 antagonist in the preparation of a medicament for the treatment of a patient with a hepcidin-mediated anemia of chronic disease,
wherein the patient has been determined to have at least one copy of the *TMPRSS6* rs855791 major allele encoding an Alanine at position 736.
2. The use of claim 1, wherein the patient is male and has a pre-treatment hemoglobin (Hb) level of less than 14 g/dl.
3. The use of claim 2, wherein the patient has a pre-treatment Hb level of less than 13 g/dl.
4. The use of claim 3, wherein the patient has a pre-treatment Hb level of less than 12 g/dl.
5. The use of claim 4, wherein the patient has a pre-treatment Hb level of less than 11 g/dl.
6. The use of claim 1, wherein the patient is female and has a pre-treatment Hb level of less than 12 g/dl.
7. The use of claim 6, wherein the patient has a pre-treatment Hb level of less than 11 g/dl.
8. The use of claim 7, wherein the patient has a pre-treatment Hb level of less than 10 g/dl.
9. The use of claim 8, wherein the patient has a pre-treatment Hb level of less than 9 g/dl.
10. The use of any one of claims 1-5, wherein the patient is male and has a pre-treatment hematocrit of less than 40%.

11. The use of claim 10, wherein the patient has a pre-treatment hematocrit of less than 35%.
12. The use of claim 11, wherein the patient has a pre-treatment hematocrit of 30 – 34%.
13. The use of any one of claims 1, 6-9, wherein the patient has a pre-treatment hematocrit of less than 36%.
14. The use of claim 13, wherein the patient has a pre-treatment hematocrit of less than 30%.
15. The use of claim 14, wherein the patient has a pre-treatment hematocrit of 26 – 29%.
16. The use of any one of claims 1 – 15, wherein the patient has received at least one pre-treatment administration of an ESA.
17. The use of claim 1, wherein the patient has received at least one pre-treatment administration of an ESA and has a normal Hb level or normal hematocrit.
18. The use of any one of claims 1 – 15, wherein the patient has received at least one pre-treatment administration of an iron supplement.
19. The use of claim 1, wherein the patient has received at least one pre-treatment administration of an iron supplement and has a normal Hb level or normal hematocrit.
20. The use of any one of claims 1 – 15, wherein the patient has received at least one pre-treatment transfusion of blood or packed red blood cells.
21. The use of claim 1, wherein the patient has received at least one pre-treatment transfusion of blood or packed red blood cells and has a normal Hb level or normal hematocrit.
22. The use of any one of claims 1 – 21, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to increase the patient's Hb levels above pre-treatment levels.

23. The use of any one of claims 1 – 22, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to increase the patient's hematocrit above pre-treatment levels.
24. The use of claim 16 or 17, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to allow reduction in the patient's dose of ESA without reduction in the patient's Hb levels below levels present immediately pre-treatment.
25. The use of claim 16 or 17, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to allow reduction in the patient's dose of ESA without reduction in the patient's hematocrit below levels present immediately pre-treatment.
26. The use of any one of claims 16, 17, 24 or 25, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to allow at least a 10% reduction in the patient's dose of ESA as compared to pre-treatment ESA dose.
27. The use of claim 26, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to allow at least a 20% reduction in the patient's dose of ESA as compared to pre-treatment ESA dose.
28. The use of claim 27, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to allow at least a 50% reduction in the patient's dose of ESA as compared to pre-treatment ESA dose.
29. The use of any one of claims 1 – 28, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reverse functional iron deficiency.
30. The use of any one of claims 1 – 29, wherein the chronic disease is chronic kidney disease (CKD).
31. The use of claim 30, wherein the patient has KDOQI stage 3 chronic kidney disease, KDOQI stage 4 chronic kidney disease, or KDOQI stage 5 chronic kidney disease.

32. The use of claim 31, wherein the patient has KDOQI stage 5 chronic kidney disease.
33. The use of claim 30, wherein the patient has cardiorenal syndrome (CRS).
34. The use of claim 33, wherein the patient has CRS Type 4.
35. The use of any one of claims 30 – 34, wherein the patient has received at least one pre-treatment dialysis treatment.
36. The use of any one of claims 30 – 35, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce cardiovascular (CV) mortality as compared to age-matched and disease-matched historical controls.
37. The use of any one of claims 1 – 29, wherein the chronic disease is a chronic inflammatory disease.
38. The use of claim 37, wherein the chronic inflammatory disease is rheumatoid arthritis (RA).
39. The use of claim 38, wherein the patient has a pre-treatment DAS28 score of greater than 5.1.
40. The use of claim 38, wherein the patient has a pre-treatment DAS28 score of 3.2 to 5.1.
41. The use of claim 38, wherein the patient has a pre-treatment DAS28 score of less than 2.6.
42. The use of claim 38, wherein the patient's pre-treatment RA is moderately active to severely active.
43. The use of any one of claims 38 – 42, wherein the patient has received at least one pre-treatment administration of methotrexate.

44. The use of any one of claims 38 – 43, wherein the patient has received at least one pre-treatment administration of a TNF α antagonist.
45. The use of claim 44, wherein the TNF α antagonist is selected from the group consisting of etanercept, adalimumab, infliximab, certolizumab, and golimumab.
46. The use of any one of claims 38 – 42, wherein the patient has received at least one pre-treatment administration of an IL-6 antagonist.
47. The use of claim 46, wherein the pre-treatment IL-6 antagonist is tocilizumab.
48. The use of claim 46, wherein the pre-treatment IL-6 antagonist is tofacitinib.
49. The use of any one of claims 46 – 48, wherein the treatment IL-6 antagonist is MEDI5117.
50. The use of claim 37, wherein the chronic inflammatory disease is selected from the group consisting of juvenile idiopathic arthritis, ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, inflammatory bowel disease, Crohn's disease, and ulcerative colitis.
51. The use of any one of claims 1 – 29, wherein the chronic disease is cancer.
52. The use of claim 51, wherein the cancer is selected from the group consisting of: solid tumors, small cell lung cancer, non-small cell lung cancer, hematological cancer, multiple myeloma, leukemias, chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), lymphomas, Hodgkin's lymphoma and hepatic adenoma.
53. The use of any one of claims 1 – 29, wherein the chronic disease is a chronic infection.
54. The use of any one of claims 1 – 29, wherein the chronic disease is congestive heart failure (CHF).
55. The use of any one of claims 1 – 29, wherein the patient has Castleman's Disease.

56. An in vitro method for determining whether an IL-6 antagonist will be ineffective in treating a patient with hepcidin-mediated anemia of chronic inflammation, the method comprising determining whether or not a nucleic acid sample obtained from the patient is homozygous for the *TMPRSS6* rs855791 minor allele, encoding a Valine at position 736.
57. The use of any one of claims 1 – 55 or the method of claim 56, wherein the patient has elevated pre-treatment serum levels of IL-6.
58. The use or method of claim 57, wherein the patient has a pre-treatment serum IL-6 level of greater than 2.5 pg/ml.
59. The use or method of claim 58, wherein the patient has a pre-treatment serum IL-6 level of greater than 5 pg/ml.
60. The use or method of claim 59, wherein the patient has a pre-treatment serum IL-6 level of greater than 7.5 pg/ml.
61. The use or method of claim 60, wherein the patient has a pre-treatment serum IL-6 level of greater than 10 pg/ml.
62. The use or method of claim 61, wherein the patient has a pre-treatment serum IL-6 level of greater than 12.5 pg/ml.
63. The use or method of any one of claims 57 – 62, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce the free IL-6 levels in the patient's serum below pre-treatment levels.
64. The use or method of claim 63, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce the free IL-6 levels by at least 10% as compared to pre-treatment levels.
65. The use or method of claim 64, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce the free IL-6 levels in the patient's serum by at least 20% as compared to pre-treatment levels.

66. The use or method of claim 65, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce the free IL-6 levels in the patient's serum by at least 50% as compared to pre-treatment levels.
67. The use of any one of claims 1 – 55 and 57 – 66 or the method of any one of claims 58 – 68, wherein the patient has elevated pre-treatment levels of C-reactive protein (CRP).
68. The use or method of claim 67, wherein the patient has a pre-treatment CRP level greater than 2 mg/L.
69. The use or method of claim 68, wherein the patient has a pre-treatment CRP level of greater than 3 mg/L.
70. The use or method of claim 69, wherein the patient has a pre-treatment CRP level of greater than 5 mg/L.
71. The use or method of claim 70, wherein the patient has a pre-treatment CRP level of greater than 7.5 mg/L.
72. The use or method of claim 71, wherein the patient has a pre-treatment CRP level of greater than 10 mg/L.
73. The use or method of any one of claims 67 – 72, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce the patient's CRP levels below pre-treatment levels.
74. The use or method of claim 73, wherein the medicament is for use at a dose, on a schedule, and for a period sufficient to reduce the patient's CRP levels by at least 50% as compared to pre-treatment levels.
75. The use of any one of claims 1 – 55 and 57 – 74 or the method of any one of claims 56 – 74, wherein the patient has been determined to have at least one copy of the *TMPRSS6* rs855791 major allele encoding an Alanine at position 736, using a real-time PCR assay.

76. The use of any one of claims 1 – 55 and 57 – 75 or the method of any one of claims 56 – 75, wherein the IL-6 antagonist is an anti-IL-6 antibody, or antigen-binding fragment or derivative thereof.
77. The use or method of claim 76, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative has a KD for binding human IL-6 of less than 100 nM.
78. The use or method of claim 77, wherein the antibody or antigen-binding fragment or derivative has a KD for binding human IL-6 of less than 50 nM.
79. The use or method of claim 78, wherein the antibody or antigen-binding fragment or derivative has a KD for binding human IL-6 of less than 10 nM.
80. The use or method of claim 79, wherein the antibody or antigen-binding fragment or derivative has a KD for binding human IL-6 of less than 1 nM.
81. The use or method of any one of claims 76 – 80, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative has an elimination half-life following intravenous administration of at least 7 days.
82. The use or method of claim 81, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative has an elimination half-life following intravenous administration of at least 14 days.
83. The use or method of claim 82, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative has an elimination half-life following intravenous administration of at least 21 days.
84. The use or method of claim 83, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative has an elimination half-life following intravenous administration of at least 30 days.

85. The use or method of any one of claims 76 – 84, wherein the IL-6 antagonist is a full-length monoclonal anti-IL-6 antibody.
86. The use or method of claim 85, wherein the antibody is an IgG1 or IgG4 antibody.
87. The use or method of claim 86, wherein the antibody is an IgG1 antibody.
88. The use or method of any one of claims 76 – 87, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative is fully human.
89. The use or method of any one of claims 76 – 87, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative is humanized.
90. The use or method of any one of claims 76 – 89, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative comprises all six variable region CDRs of MED5117.
91. The use or method of claim 90, wherein the antibody comprises the VH and VL of MED5117.
92. The use or method of claim 91, wherein the antibody is MED5117.
93. The use or method of any one of claims 76 – 89, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative comprises all six variable region CDRs of an antibody selected from the group consisting of siltuximab, gerilimzumab, sirukumab, clazakizumab, olokizumab, elsilimomab, VX30 (VOP-R003; Vaccinex), EB-007 (EBI-029; Eleven Bio), ARGX-109 (ArGEN-X), FM101 (Femta Pharmaceuticals, Lonza) and ALD518/BMS-945429 (Alder Biopharmaceuticals, Bristol-Myers Squibb).
94. The use or method of claim 93, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative comprises the heavy chain V region and light chain V region from an antibody selected from the group consisting of siltuximab, gerilimzumab, sirukumab, clazakizumab, olokizumab, VX30 (VOP-R003; Vaccinex), EB-007 (EBI-029; Eleven Bio), ARGX-109 (ArGEN-X), FM101 (Femta Pharmaceuticals, Lonza) and ALD518/BMS-945429 (Alder Biopharmaceuticals, Bristol-Myers Squibb).

95. The use or method of claim 94, wherein the anti-IL-6 antibody or antigen-binding fragment or derivative is an antibody selected from the group consisting of siltuximab, gerilimumab, sirukumab, clazakizumab, olokizumab, VX30 (VOP-R003; Vaccinex), EB-007 (EBI-029; Eleven Bio), ARGX-109 (ArGEN-X), FM101 (Femta Pharmaceuticals, Lonza) and ALD518/BMS-945429 (Alder Biopharmaceuticals, Bristol-Myers Squibb).
96. The use or method of any one of claims 76 – 84, wherein the IL-6 antagonist is a single domain antibody, a VHH Nanobody, an Fab, or a scFv.
97. The use of any one of claims 1 – 55 and 57 – 75 or the method of any one of claim 56 – 75, wherein the IL-6 antagonist is an anti-IL-6R antibody, or antigen-binding fragment or derivative thereof.
98. The use or method of claim 97, wherein the anti-IL-6R antibody, antigen-binding fragment, or derivative is tocilizumab.
99. The use or method of claim 98, wherein the anti-IL-6R antibody, antigen-binding fragment, or derivative is vobarilizumab.
100. The use of any one of claims 1 – 55 and 57 – 75 or the method of any one of claims 58 – 77, wherein the IL-6 antagonist is a JAK inhibitor.
101. The use or method of claim 100, wherein the JAK inhibitor is selected from the group consisting of tofacitinib (Xeljanz), decernotinib, ruxolitinib, upadacitinib, baricitinib, filgotinib, lestaurtinib, pacritinib, peficitinib, INCB-039110, ABT-494, INCB-047986 and AC-410.
102. The use of any one of claims 1 – 55 and 57 – 75 or the method of any one of claims 58 – 77, wherein the IL-6 antagonist is a STAT3 inhibitor.
103. The use or method of any one of claims 76 – 99, wherein the medicament is for use parenterally.

104. The use or method of claim 102, wherein the medicament is for use subcutaneously.
105. The use or method of claim 100 or claim 101, wherein the medicament is for use orally.